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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,008	01/02/2001	Stefan Somlo	96700/658	1280

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,008	SOMLO ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/9/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on January 18, 2005 has been entered. The claims pending in this application are claims 76-81. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn. Since the examiner notes that newly found rejections must be made, **PROSECUTION IS HEREBY REOPENED**. New grounds of rejection are set forth below. Therefore, claims 76-81 will be examined.

Information Disclosure Statement

2. Since applicant has provided a legible copy of the reference (San Millan et al., Am. J. Hum. Genet, 1995, 56(1): 248-53), the information disclosure statement filed on July 7, 2004 has complied with 37 CFR 1.98(a)(2). The examiner has signed the form 1449 filed on July 9, 2004 and attached signed form 1449 with this office action.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 76-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed". *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification provides adequate written description for three human families with certain kind of point mutations in human PKD2 gene (see Figure 3 and Figures 5A to 5G). However, the specification fails to adequately describe any kind of mutations in human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene recited in claims 76-81. The claimed inventions as a whole are not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed inventions as a whole) such that a

person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, mutations recited in claims 76-81 are read as any kind of mutations in human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene. Although the specification provides adequate written description for three human families with certain kind of point mutations in human PKD2 gene (see Figure 3 and Figures 5A to 5G), the specification fails to adequately describe any kind of mutations in human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene. It is unclear, besides point mutations in human PKD2 gene shown Figure 3 of the specification, whether any kind of mutations in human PKD2 gene recited in the claims exists in nature. Furthermore, it is unclear whether human PKD2 gene with a large deletion or insertion can still be called as human PKD2 gene. Therefore, mutations of PKD2 gene which comprise one or more deletion, insertion, point or rearrangement mutations as recited in claims 76-81 encompass numerous unknown and unidentified mutations of PKD2 gene that miss from the disclosure. Therefore, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all possible mutations of PKD2 gene with unknown and unidentified properties and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See

Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5. Claims 76-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the methods recited in claims 76-81 to detect certain specific point mutations of human PKD2 gene when polynucleotide samples from human subjects contain certain specific point mutations of human PKD2 gene, does not reasonably provide enablement for the methods recited in claims 76-81 to detect any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene when polynucleotide samples from human subjects do not contain any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to

be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance to show that the methods recited in claims 76-81 can be used to detect any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene when polynucleotide samples from human subjects do not contain any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 76-81 can be can be used to detect any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene.

Claims 76-81 are directly to a method of detecting the presence or absence of a mutation in the sequence of human PKD2 gene. The specification only provides guidance for detecting specific point mutations in human PKD2 gene using PCR products from three human families (see Figure 3). However, the specification does not provide guidance for detecting any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutation in human PKD2 gene. Because the

specification does not describe polynucleotide samples from human subjects containing any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene, it is unpredictable whether the method recited in claims 76-81 can be used to detect any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene. It is unclear whether human PKD2 gene with any kind of deletion or insertion exists in nature and whether and human PKD2 gene with any kind of point or rearrangement mutations exists in nature. Furthermore, it is unclear whether human PKD2 gene with a large deletion or insertion can still be called as human PKD2 gene.

With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentations at least includes to test whether that the methods recited in claims 76-81 can be used to detect any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene when polynucleotide samples from human subjects do not contain any kind of mutations of human PKD2 gene including any kind of deletion and insertion in human PKD2 gene, and any kind of point or rearrangement mutations in human PKD2 gene.

Conclusion

6. No claim is allowed.

7. Claims 76-81 appear to be allowable if applicant agrees to rewrite the claims 76 and 81 as following:

76. A method of detecting the presence or absence of a mutation in the sequence of polycystic kidney disease type 2 (PKD2) gene (SEQ ID NO: 6) in a human subject, comprising the steps of:

(a) obtaining a polynucleotide sample from a human subject containing [the sequence] a suspected point mutation of PKD2 gene [from a human subject] wherein said suspected point mutation is selected from the group consisting of G to A at nucleotide 1205 of SEQ ID NO: 6, C to T at nucleotide 2290 of SEQ ID NO: 6, and C to T at nucleotide 1279 of SEQ ID NO: 6;

(b) comparing PKD2 gene sequence of the polynucleotide sample to a reference human wild-type PKD2 sequence consisting of SEQ ID NO: 6; and

(c) [determining the differences, if any, between] detecting said suspected point mutation in the sequence of PKD2 gene [in the polynucleotide sample and the reference wild-type PKD2 sequence[,wherein the differences are mutations of PKD2 gene which comprise one or more deletion, insertion, point, or rearrangement mutations;] indicates the presence of said suspected point mutation [thereby detecting the presence or absence of a mutation in the sequence] of PKD2 gene in a human subject.

79. A method of detecting the presence or absence of a mutation in the sequence of in the sequence of polycystic kidney disease type 2 (PKD2) gene (SEQ ID NO: 6)
in a human subject, comprising the steps of:

(a) obtaining a polynucleotide sample from a human subject containing [the sequence] a suspected point mutation of PKD2 gene [from a human subject] wherein said suspected point

mutation is selected from the group consisting of G to A at nucleotide 1205 of SEQ ID NO: 6, C to T at nucleotide 2290 of SEQ ID NO: 6, and C to T at nucleotide 1279 of SEQ ID NO: 6; and (b) performing sequence analysis of the polynucleotide sample [to detect the presence or absence of a mutation in the sequence of PKD2 gene of the human subject, wherein the mutation comprises a deletion, insertion, point, or rearrangement mutations] and detecting said suspected point mutation in the sequence of PKD2 gene indicates the presence of said suspected point mutation of PKD2 gene in a human subject.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
March 7, 2005

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